

U.S.S.N. 09/139,425

Filed: August 25, 1998

CLEAN VERSION OF AMENDMENTS PURSUANT TO 37 C.F.R. § 1.121

Clean Version of Amended Claims

Pursuant to 37 C.F.R. § 1.121(c)(1)(iii)

1. (three times amended) A method for selectively delivering molecules to the nucleus of endothelial cells of the large vessels, comprising

administering a conjugate of an agent binding selectively to endothelial protein C receptor (EPCR) and the molecule to be delivered to large vessel endothelial cells, wherein the molecules are delivered to the nucleus of the large vessel endothelial cells.

2. The method of claim 1 wherein the conjugate is formed between the molecule to be delivered and an antibody to EPCR.

3. The method of claim 1 wherein the conjugate is formed between the molecule to be delivered and activated protein C.

4. The method of claim 1 wherein the conjugate comprises a chimeric antibody binding to the molecule to be delivered and to EPCR.

5. (four times amended) The method of claim 1 wherein the molecule to be delivered is a nucleic acid molecule and the nucleic acid molecule is a gene or cDNA under the control of a promoter expressed in the nucleus of an endothelial cell and the nucleic acid molecule is delivered by directly contacting the endothelial cells of large vessels with the nucleic acid molecule conjugate or by catheterization to the endothelial cells.

6. (twice amended) The method of claim 5 wherein the nucleic acid molecule is selected from the group consisting of triplex forming oligonucleotides, ribozymes, guide sequences for ribozymes, and antisense.

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7. (Twice Amended) The method of claim 1 wherein the molecule to be delivered is selected from the group consisting of drugs other than nucleic acids and proteins and diagnostic agents.
8. The method of claim 1 wherein the molecule to be delivered is a protein.
9. The method of claim 8 wherein the protein is a transcription factor.
10. The method of claim 1 wherein the molecule to be delivered is coupled to the agent which binds to EPCR by molecules selected from the group consisting of streptavidin and biotin, and molecules having multiple positive charges.
11. The method of claim 1 wherein the conjugate is administered to large vessel endothelial cells in culture or isolated from an individual.
12. (amended) The method of claim 1 wherein the conjugate is administered directly to the cells of to an individual in need of treatment or diagnosis.
13. (amended) A conjugate of an agent binding selectively to endothelial protein C receptor (EPCR) selected from the group consisting of protein C, activated protein C, antibodies reactive with EPCR and fragments thereof binding to EPCR, and a molecule to be delivered to a large vessel endothelial cell, wherein the molecule is not a diagnostic label, wherein the conjugate is a chemical conjugate, fusion protein or conjugate formed by indirect binding by a positively charged polymer, chimeric antibody or streptavidin.
14. The conjugate of claim 13 wherein the conjugate is formed with an antibody to EPCR, or a fragment or recombinant molecule based thereon, binding to EPCR.

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15. The conjugate of claim 13 wherein the conjugate is formed between the agent to be delivered and activated protein C.
16. (four times amended) The conjugate of claim 13 wherein the molecule to be delivered is a nucleic acid molecule in combination with means for directly contacting the nucleic acid molecule conjugate directly with the endothelial cells of large vessels, wherein the means are for in vitro treatment of the cells or by catheterization to the endothelial cells.
17. (twice amended) The conjugate of claim 16 wherein the nucleic acid molecule is a gene or cDNA under the control of a promoter expressed in the nucleus of an endothelial cell.
18. (twice amended) The conjugate of claim 16 wherein the nucleic acid molecule is selected from the group consisting of triplex forming oligonucleotides, ribozymes, guide sequences for ribozymes, and antisense.
19. (Three Times Amended) The conjugate of claim 13 wherein the molecule to be delivered is a drug other than nucleic acids and proteins.
20. The conjugate of claim 13 wherein the molecule to be delivered is a protein.
21. The conjugate of claim 20 wherein the protein is a transcription factor.
22. The conjugate of claim 20 comprising a coupling means which binds the molecule to be delivered to the agent which binds EPCR.
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~~22~~. The conjugate of claim 22 wherein the coupling means is a positively charged polymer or molecule.
24. The conjugate of claim 22 wherein the coupling means is streptavidin-biotin.

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25. The conjugate of claim 13 comprising a chimeric antibody which binds to EPCR and to the molecule to be delivered.